Questions for the Panel

InSync Model 7272 ICD System

Study Design and Analysis Method

1. Please comment on the sponsor's study design. Specifically, please address the following issues in your discussion:
   a. Please comment on the adequacy of the sample size that contributed data in support of the primary endpoints. In particular, are there any concerns related to the "administrative censoring" of 20 percent of the enrolled patients who had not passed the 6-month point at the time of the submission?
   b. Please discuss the benefits and limitations associated with the 6-month follow-up duration for the primary endpoints.
   c. Please discuss the propensity for crossovers and any additional issues that may be related to blinding.
   d. The intent-to-treat analysis on NYHA Class, Quality of Life, and 6-Minute Hall Walk produced nominal p-values of 0.027, 0.009, and 0.407, respectively. Thus, the study results meet the pre-specified Hochberg criteria for statistical significance in that one of the endpoints (Quality of Life) produced a p-value less than 0.0167. In light of this, please comment on the possible interpretation of the results for each of the co-primary endpoints individually.

Effectiveness of the System in Treating CHF

2. The primary endpoints of the study were improvement in NYHA Class, Quality of Life, and 6-Minute Hall Walk. Please discuss the clinical relevance of these endpoints for evaluating a therapy for congestive heart failure (CHF).

3. Please discuss the clinical relevance of the sponsor's choice of secondary endpoints for evaluating a therapy for CHF. Are there specific secondary endpoints, such as peak VO_2, that should be more heavily weighted in the assessment of the device?

4. Please comment on whether the results of the clinical study support the effectiveness of the device for the treatment of patients with medically stable Class III/IV CHF.

Safety of the System in Treating CHF

5. When evaluating the safety of the device, one concern is whether the treatment contributes to the worsening of CHF. The sponsor has identified several measures designed to capture this including the CHF Composite Response, hospitalizations, medication changes, and mortality. Please comment on whether the results support the safety of the system for treating CHF in the population studied.

Effectiveness of the System as an ICD

6. Please comment on whether the sponsor has provided adequate information to assure that there is no interference of proper ICD functionality with the addition of biventricular pacing, and that both biventricular pacing and ICD therapy can be delivered simultaneously.

7. Please discuss whether you have any comments or recommendations regarding programming considerations for the device.

Safety of the System

8. For the Model 7272 ICD pulse generator, the sponsor has provided analyses of the ICD system-related complications at 3 months. Please comment on whether the results provide a reasonable assurance of the safety of the Model 7272 ICD pulse generator.

9. For the Model 4189 Lead, the sponsor has provided analyses of lead-related complications at 6 months. Please comment on whether the results provide a reasonable assurance of the safety of the Model 4189 Lead.

10. The sponsor has provided analyses of the system-related complications at 6-months and the adverse events (complications and observations) reported in the clinical study. Please comment on whether the results provide a reasonable assurance of the safety of the InSync ICD System.

Risk-Benefit of the System for Treatment of CHF

11. FDA defines safety as reasonable assurance that the probable benefits to health outweigh any probable risks. Effectiveness is defined as reasonable assurance that, in a significant portion of the population, the use of the device for its intended uses will provide clinically significant results. Please discuss the overall risk-benefit of the system.

Labeling

12. One aspect of the pre-market evaluation of a new product is the review of its labeling. The labeling must indicate which patients are appropriate for treatment, identify potential adverse events with the use of the device, and explain how the product should be used to maximize benefits and minimize adverse effects. If you recommend approval of the device, please address the following questions regarding product labeling.
    a. Do the INDICATIONS FOR USE adequately define the patient population studied?
    b. Based on the clinical experience, should there be additional CONTRAINDICATIONS, WARNINGS and PRECAUTIONS for the use of the InSync Model 7272 ICD System?
    c. Please comment on the operator instructions as to whether they adequately describe how the device should be used to maximize the benefits and minimize adverse events.
    d. Please provide any other recommendations or comments regarding the labeling of this device.

Post-Market Study

13. With approval of the Medtronic InSync biventricular pacing system, FDA and the sponsor agreed on the following post-approval conditions: a) obtaining 12-month mortality data on the IDE cohort, and b) performing a 3-year evaluation of mortality and chronic lead performance, including electrical performance and adverse events, on 1,000 patients. If you recommend approval, please comment on whether additional clinical follow-up or post-market studies are necessary for this device.